

NMCP COVID-19 Literature Report #36: Friday, 21 August 2020

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Purpose: These now weekly reports, published on Fridays, are curated collections of current research, evidence reviews, and news regarding the COVID-19 pandemic. Please feel free to reach out with questions, suggestions for future topics, or any other concerns.

All reports are available online at <https://nmcp.libguides.com/covidreport>. Access is private; you will need to use the direct link or bookmark the URL, along with the case-sensitive password "NMCPfinest".

Disclaimer: I am not a medical professional. This document is current as of the date noted above. While I make every effort to find and summarize available data, things are changing rapidly, with new research and potentially conflicting literature published daily.

Statistics

Global today: 22,726,945 confirmed cases and 794,466 deaths in 188 countries/regions

last report: 20,960,424 confirmed cases and 760,371 deaths in 188 countries/regions

United States*

top 5 states by cases (Virginia is ranked 16th)

	TOTAL US	CA	FL	TX	NY	GA
Confirmed Cases	5,579,142	653,637	588,602	579,892	428,512	246,741
Tested	70,031,936	10,227,966	4,335,752	4,547,069	7,353,387	2,096,835
Recovered	NA	NA	NA	431,960	74,406	NA
Deaths	174,306	11,837	10,049	11,174	32,861	4,904

*see census.gov for current US Population data; NA: not all data available

[JHU CSSE](https://www.jhu.edu/) as of 1100 EDT 21 August 2020

Virginia	Total	Chesapeake	Hampton	Newport News	Norfolk	Portsmouth	Suffolk	Virginia Beach
Cases	110,860	3,412	1,417	2,072	4,119	2,057	1,503	5,623
Hospitalized	9,071	277	53	83	251	156	112	298
Deaths	2,436	41	10	20	39	30	57	61

[VA DOH](https://www.vahhs.org/) as of 1100 EDT 21 August 2020

Special Reports

[JHCHS](#): Interim Framework for COVID-19 Vaccine Allocation and Distribution in the United States (posted 19 August 2020)

"The COVID-19 pandemic will continue for the foreseeable future, but widespread vaccination could hasten its end. At least 165 candidate vaccines for the SARS CoV-2 virus are in development around the world and there is hope that one or more of these candidates will soon be shown to be sufficiently safe and effective to achieve emergency use authorization in the United States. When a vaccine has been authorized for use, it will initially be in limited supply. During this period of scarcity, a plan is needed for how to allocate and distribute the limited supply—which groups should be prioritized to receive the vaccine first and which groups can wait until later. This difficult and potentially contentious topic is being actively discussed in the United States by the Advisory Committee on Immunization Practices (ACIP) of the US Centers for Disease Control and Prevention (CDC) and the National Academy of Medicine (NAM), as well as globally at the World Health Organization (WHO) and elsewhere. The purpose of this report is to offer an additional ethics framework for use in making decisions about allocation of SARS-CoV-2 vaccine during this initial period of scarcity in the United States and make related suggestions about vaccine distribution. Our approach takes into account considerations of medical risk, public health, ethics and equity, economic impact, and logistics. We note where our approach aligns or differs from the 2018 CDC guidance for vaccine allocation in a severe influenza pandemic, which is the most recent pandemic vaccine guidance from the US government.

This report is the product of deliberations of a multi-disciplinary team of public health experts at Johns Hopkins University including members from the Center for Health Security, the Berman Institute for Bioethics, The Armstrong Institute for Patient Safety and Quality, the International Vaccine Access Center, the Center for Vaccine Research, in the Johns Hopkins Schools of Public Health, Medicine, and Nursing. The deliberations were informed by a review of available literature and open source government documents. We were not privy to any proprietary or unpublished information that may be available to other groups considering these issues that could alter judgments about prioritization, and acknowledge the evolving state of the evidence about pathogenesis and vaccine response. Therefore, our suggested priority groups should be viewed only as plausible examples of candidates for top tier prioritization when applying the framework, and not as definitive recommendations.

The intended audience for this report includes policy makers and technical experts in the US federal government currently working on vaccine allocation plans, those at the state and local levels who will be implementing allocation plans, community leaders, activists and the general public interested in influencing vaccine allocation decisions. The principal product of this report is an ethical framework to guide discussion and inform decisions about vaccine allocation. This framework places emphasis on promoting the common good, by promoting public health and also by enabling social and economic activity. It also emphasizes the

importance of treating individuals fairly and promoting social equity, for example by addressing racial and ethnic disparities in COVID mortality, and by recognizing the contributions of essential workers who have been overlooked in previous allocation schemes. The framework also includes a third ethical value not often well-articulated in ethics discussions of vaccine allocation and whose importance we wish to elevate—the promotion of legitimacy, trust and a sense of community ownership over vaccine policy, while respecting the diversity of values and beliefs in our pluralist society. We consider the ethical principles that should guide COVID-19 vaccine allocation and identify more specific policy goals and objectives that follow from these ethical principles."

[DHS](#): Master Question List for COVID-19 (caused by SARS-CoV-2) (18 August 2020)

"The Department of Homeland Security (DHS) Science and Technology Directorate (S&T) developed the following "master question list" that quickly summarizes what is known, what additional information is needed, and who may be working to address such fundamental questions as, "What is the infectious dose?" and "How long does the virus persist in the environment?" The Master Question List (MQL) is intended to quickly present the current state of available information to government decision makers in the operational response to COVID-19 and allow structured and scientifically guided discussions across the federal government without burdening them with the need to review scientific reports, and to prevent duplication of efforts by highlighting and coordinating research."

Evidence Summaries

[CEBM](#): Advance care planning in the community in the context of COVID-19 (published 18 August 2020)

- "In the context of COVID-19, some known barriers to advance care planning (ACP) in community settings have worsened, while others have improved. The same is true for known enablers of ACP (Table 1).
- COVID-19 has raised public awareness of ACP, increased the importance of and attention to IT systems, motivated the development of new guidelines and templates, and rapidly shifted 'business as usual' processes and protocols. This presents opportunities to improve ACP in the community.
- However, existing guidelines and resources are to a major extent clinician-focused; there are few video- and web-based ACP resources for the public and those that exist are scattered and piecemeal. This is a concern given good quality evidence that online and video ACP interventions are beneficial, particularly among people with limited English proficiency, poor health literacy and/or from otherwise disadvantaged communities.

- In the context of COVID-19, and to reduce inequalities in access to ACP, we recommend national investment in evidence-based, public-facing resources and integrated systems to support ACP, building on existing resources.
- Alongside this investment, simultaneous, interconnected strategies are needed, underpinned by healthcare policy: training for those working in health and social care, better coordination of electronic medical record systems, and public education and awareness raising."

Selected Literature: Peer-Reviewed Journals

Date given is the date published or posted online; often these papers are ahead of print.

19 August 2020

[BMJ](#): Face coverings for covid-19: from medical intervention to social practice

- "Face coverings used by the public are now widely recommended as source control during the covid-19 pandemic
- The dominant narrative driving policy has viewed face coverings as a medical intervention and evaluated their effectiveness from an infection control perspective
- Face coverings are also a social practice and carry a range of meanings in different settings
- Policies to encourage uptake should reflect the complex and contested sociocultural meanings of covering the face and draw on these to promote their use"

[J Antimicrob Chemother](#): The impact of sofosbuvir/daclatasvir or ribavirin in patients with severe COVID-19

"Patients with a positive nasopharyngeal swab for SARS-CoV-2 on RT-PCR or bilateral multi-lobar ground-glass opacity on their chest CT and signs of severe COVID-19 were included. Subjects were divided into two arms with one arm receiving ribavirin and the other receiving sofosbuvir/daclatasvir. All participants also received the recommended national standard treatment which, at that time, was lopinavir/ritonavir and single-dose hydroxychloroquine....

The median duration of stay was 5 days for the sofosbuvir/daclatasvir group and 9 days for the ribavirin group. The mortality in the sofosbuvir/daclatasvir group was 2/35 (6%) and 9/27 (33%) for the ribavirin group. The relative risk of death for patients treated with sofosbuvir/daclatasvir was 0.17 (95% CI 0.04–0.73, $P = 0.02$) and the number needed to treat for benefit was 3.6 (95% CI 2.1–12.1, $P < 0.01$)."

[J Antimicrob Chemother](#): Sofosbuvir and daclatasvir compared with standard of care in the treatment of patients admitted to hospital with moderate or severe coronavirus infection (COVID-19): a randomized controlled trial

"This was an open-label, multicentre, randomized controlled clinical trial in adults with moderate or severe COVID-19 admitted to four university hospitals in Iran. Patients were randomized into a treatment arm receiving sofosbuvir and daclatasvir plus standard care, or a control arm receiving standard care alone....

The addition of sofosbuvir and daclatasvir to standard care significantly reduced the duration of hospital stay compared with standard care alone. Although fewer deaths were observed in the treatment arm, this was not statistically significant. Conducting larger scale trials seems prudent."

[J Pediatr](#): Pediatric SARS-CoV-2: Clinical Presentation, Infectivity, and Immune Responses

"Children ages 0-22 years with suspected severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection presenting to urgent care clinics or being hospitalized for confirmed/suspected SARS-CoV-2 infection or multisystem inflammatory syndrome in children (MIS-C) at Massachusetts General Hospital (MGH) were offered enrollment in the MGH Pediatric COVID-19 Biorepository. Enrolled children provided nasopharyngeal, oropharyngeal, and/or blood specimens. SARS-CoV-2 viral load, ACE2 RNA levels, and serology for SARS-CoV-2 were quantified.

A total of 192 children (mean age 10.2 +/- 7 years) were enrolled. Forty-nine children (26%) were diagnosed with acute SARS-CoV-2 infection; an additional 18 children (9%) met criteria for MIS-C. Only 25 (51%) of children with acute SARS-CoV-2 infection presented with fever; symptoms of SARS-CoV-2 infection, if present, were non-specific. Nasopharyngeal viral load was highest in children in the first 2 days of symptoms, significantly higher than hospitalized adults with severe disease ($P = .002$). Age did not impact viral load, but younger children had lower ACE2 expression ($P=0.004$). IgM and IgG to the receptor binding domain (RBD) of the SARS-CoV-2 spike protein were increased in severe MIS-C ($P<0.001$), with dysregulated humoral responses observed.

This study reveals that children may be a potential source of contagion in the SARS-CoV-2 pandemic in spite of milder disease or lack of symptoms, and immune dysregulation is implicated in severe post-infectious MIS-C."

[JAMA](#): Evaluation for SARS-CoV-2 in Breast Milk From 18 Infected Women

"Concern has been raised that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) may be transmitted to infants by breastfeeding. A number of organizations advise that women infected with SARS-CoV-2 may choose to breastfeed with protections to prevent transmission of the virus through respiratory droplets. Of 24 case reports on breast milk samples from women infected with SARS-CoV-2, viral RNA was detected in 10 samples from

4 women. In some cases, environmental contamination or retrograde flow from an infected infant could not be ruled out. Detection of viral RNA by reverse transcriptase–polymerase chain reaction (RT-PCR) does not equate with infectivity. To date, SARS-CoV-2 has not been isolated from breast milk, and there are no documented cases of transmission of infectious virus to the infant through breast milk. However, potential for viral transmission through breast milk remains a critical question for women infected with SARS-CoV-2 who wish to breastfeed....

Although SARS-CoV-2 RNA was detected in 1 milk sample from an infected woman, the viral culture for that sample was negative. These data suggest that SARS-CoV-2 RNA does not represent replication-competent virus and that breast milk may not be a source of infection for the infant. Furthermore, when control samples spiked with replication-competent SARS-CoV-2 virus were treated by Holder pasteurization, no replication-competent virus or viral RNA was detectable. These findings are reassuring given the known benefits of breastfeeding and human milk provided through milk banks."

[MMWR](#): COVID-19 Among American Indian and Alaska Native Persons — 23 States, January 31–July 3, 2020

"American Indian and Alaska Native (AI/AN) persons appear to be disproportionately affected by the COVID-19 pandemic; however, limited data are available to quantify the disparity in COVID-19 incidence, severity, and outcomes among AI/AN persons compared with those among other racial/ethnic groups.

In 23 states with adequate race/ethnicity data, the cumulative incidence of laboratory-confirmed COVID-19 among AI/AN persons was 3.5 times that among non-Hispanic white persons. A large percentage of missing data precluded analysis of some characteristics and outcomes.

Adequate health care and public health infrastructure resources are needed to support a culturally responsive public health effort that sustains the strengths of AI/AN communities. These resources would facilitate the collection and reporting of more complete case report data to support evidence-based public health efforts."

18 August 2020

[Eur Resp J](#): Elevated ACE2 expression in the olfactory neuroepithelium: implications for anosmia and upper respiratory SARS-CoV-2 entry and replication

"ACE2 protein is expressed at high levels in the human olfactory epithelium relative to upper airway epithelial cells. This may explain COVID-19-associated olfactory dysfunction, while suggesting a SARS-CoV-2 reservoir site and potential intranasal therapy."

Previously posted as preprint:

<https://www.biorxiv.org/content/10.1101/2020.05.08.084996v1>

[J Eur Acad Dermatol Venereol](#): Scabies outbreak during home confinement due to the SARS-CoV-2 pandemic

"In response to the rapid spread of COVID-19 at the start of the pandemic, governments introduced severe measures of home confinement and isolation of the population in an effort to prevent their health systems from collapsing....

In recent weeks, numerous articles have reported a wide range of skin symptoms of COVID-19, but there are other dermatological conditions that may have been aggravated during this global pandemic. Scabies is a highly contagious skin infestation caused by the mite *Sarcoptes scabiei* (variety *hominis*).... [W]e have observed a significant increase of scabies cases in our region [of Spain] during the confinement period (March, April and May 2020) compared to the average for the same period during the previous five years (64 vs. 18.6 patients)."

[JAMA Intern Med](#): Evaluating the Association of Clinical Characteristics With Neutralizing Antibody Levels in Patients Who Have Recovered From Mild COVID-19 in Shanghai, China

"Question: Are clinical characteristics of patients who recovered from mild coronavirus disease 2019 (COVID-19) associated with levels of neutralizing antibodies?

Findings: In this cohort study of 175 patients who recovered from mild COVID-19, neutralizing antibody titers to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) varied substantially at the time of discharge. In addition, neutralizing antibodies were not detected in 10 patients.

Meaning: Further research is needed to understand the implications of variable levels of SARS-CoV-2-specific neutralizing antibodies for protection against future infections with SARS-CoV-2."

[JAMA Netw Open](#): Assessment of SARS-CoV-2 Transmission on an International Flight and Among a Tourist Group

"This case series assessed a commercial airline flight from Tel Aviv, Israel, to Frankfurt, Germany, that occurred on March 9th, 2020. Among 102 passengers on a Boeing 737-900 aircraft were 24 members of a tourist group. Starting 7 days earlier, the group had contact with a hotel manager who later received a diagnosis of coronavirus disease 2019 (COVID-19). No member of the group had received a diagnosis of COVID-19 before the flight, and no measures to prevent transmission (eg, wearing of masks) had been applied. The flight duration was 4 hours 40 minutes....

We discovered 2 likely SARS-CoV-2 transmissions on this flight, with 7 index cases. These transmissions may have also occurred before or after the flight. The risk of transmission of droplet-mediated infections on an aircraft depends on proximity to an index case and on other factors, such as movement of passengers and crew, fomites, and contact among

passengers in the departure gate. In our study, both passengers with likely onboard transmission were seated within 2 rows of an index case."

[JAMA Netw Open](#): Association of Race With Mortality Among Patients Hospitalized With Coronavirus Disease 2019 (COVID-19) at 92 US Hospitals

"Question: Is race associated with mortality among patients hospitalized with coronavirus disease 2019 (COVID-19) in the United States?

Findings: In this cohort study of 11 210 individuals with COVID-19 presenting for care at 92 hospitals across 12 states, there was no difference in all-cause, in-hospital mortality between White and Black patients after adjusting for age, sex, insurance status, comorbidity, neighborhood deprivation, and site of care.

Meaning: In this study, race was not independently associated with in-hospital mortality after adjusting for differences in sociodemographic and clinical factors."

[Lancet](#): Effects of a major deletion in the SARS-CoV-2 genome on the severity of infection and the inflammatory response: an observational cohort study

"Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants with a 382-nucleotide deletion (Δ 382) in the open reading frame 8 (ORF8) region of the genome have been detected in Singapore and other countries. We investigated the effect of this deletion on the clinical features of infection.

We retrospectively identified patients who had been screened for the Δ 382 variant and recruited to the PROTECT study—a prospective observational cohort study conducted at seven public hospitals in Singapore. We collected clinical, laboratory, and radiological data from patients' electronic medical records and serial blood and respiratory samples taken during hospitalisation and after discharge. Individuals infected with the Δ 382 variant were compared with those infected with wild-type SARS-CoV-2. Exact logistic regression was used to examine the association between the infection groups and the development of hypoxia requiring supplemental oxygen (an indicator of severe COVID-19, the primary endpoint). Follow-up for the study's primary endpoint is completed.

Between Jan 22 and March 21, 2020, 278 patients with PCR-confirmed SARS-CoV-2 infection were screened for the Δ 382 deletion and 131 were enrolled onto the study, of whom 92 (70%) were infected with the wild-type virus, ten (8%) had a mix of wild-type and Δ 382-variant viruses, and 29 (22%) had only the Δ 382 variant. Development of hypoxia requiring supplemental oxygen was less frequent in the Δ 382 variant group (0 [0%] of 29 patients) than in the wild-type only group (26 [28%] of 92; absolute difference 28% [95% CI 14–28]). After adjusting for age and presence of comorbidities, infection with the Δ 382 variant only was associated with lower odds of developing hypoxia requiring supplemental oxygen (adjusted odds ratio 0.07 [95% CI 0.00–0.48]) compared with infection with wild-type virus only.

The $\Delta 382$ variant of SARS-CoV-2 seems to be associated with a milder infection. The observed clinical effects of deletions in ORF8 could have implications for the development of treatments and vaccines."

17 August 2020

[JAMA Intern Med](#): Assessment of COVID-19 Hospitalizations by Race/Ethnicity in 12 States

"This analysis identified considerable disparities in the prevalence of COVID-19 across racial/ethnic subgroups of the population in 12 US states. These findings are consistent with an earlier Centers for Disease Control and Prevention analysis of 580 hospitalizations between March 1 and March 30, 2020, that found disproportionately high COVID-19 hospitalizations for the Black population. Similarly, a study of 1052 confirmed COVID-19 cases between January 1 and April 8, 2020, at a California health system reported higher odds of hospitalization in non-Hispanic Black individuals compared with non-Hispanic White individuals. In addition, we observed high hospitalization rates for Hispanic individuals in most of the states analyzed and high hospitalization rates for American Indian and Alaskan Native populations in select states."

[MMWR](#): Racial and Ethnic Disparities Among COVID-19 Cases in Workplace Outbreaks by Industry Sector — Utah, March 6–June 5, 2020

"During March 6–June 5, 2020, workplace outbreaks occurred in 15 Utah industry sectors; 58% of workplace outbreak-associated COVID-19 cases were in three sectors: Manufacturing, Wholesale Trade, and Construction. Despite representing 24% of Utah workers in all affected sectors, Hispanic and nonwhite workers accounted for 73% of workplace outbreak-associated COVID-19 cases.

Sector-specific COVID-19 guidance should be followed. Mitigation strategies should be culturally and linguistically responsive to racial/ethnic minority workers disproportionately affected by COVID-19. Collection of detailed case occupation data is needed to understand types of work where exposure risk is highest."

[Nat Med](#): Peripheral immunophenotypes in children with multisystem inflammatory syndrome associated with SARS-CoV-2 infection

"Recent reports highlight a new clinical syndrome in children related to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)—multisystem inflammatory syndrome in children (MIS-C)—which comprises multiorgan dysfunction and systemic inflammation. We performed peripheral leukocyte phenotyping in 25 children with MIS-C, in the acute (n = 23; worst illness within 72 h of admission), resolution (n = 14; clinical improvement) and convalescent (n = 10; first outpatient visit) phases of the illness and used samples from seven age-matched healthy controls for comparisons. Among the MIS-C cohort, 17 (68%) children were SARS-CoV-2 seropositive, suggesting previous SARS-CoV-2 infections, and these children had more severe disease. In the acute phase of MIS-C, we observed high

levels of interleukin-1 β (IL-1 β), IL-6, IL-8, IL-10, IL-17, interferon- γ and differential T and B cell subset lymphopenia. High CD64 expression on neutrophils and monocytes, and high HLA-DR expression on $\gamma\delta$ and CD4+CCR7+ T cells in the acute phase, suggested that these immune cell populations were activated. Antigen-presenting cells had low HLA-DR and CD86 expression, potentially indicative of impaired antigen presentation. These features normalized over the resolution and convalescence phases. Overall, MIS-C presents as an immunopathogenic illness and appears distinct from Kawasaki disease."

15 August 2020

[J Infect](#): The dilemma of COVID-19 recurrence after clinical recovery

Letter to the editor in response to [Batisse et al. \(30 June 2020\)](#) commenting on the suggestion of reactivation or reinfection of COVID-19. It includes data of a cohort of COVID-19 patients in Italy that had recurrence, according to the authors: "In conclusion, our data confirm that recurrence of COVID-19 infection is a fairly frequent phenomenon. Little is known on how to manage these patients and how this will impact the evolution of the pandemic in the future."

14 August 2020

[Cell](#): Robust T cell immunity in convalescent individuals with asymptomatic or mild COVID-19

"SARS-CoV-2-specific memory T cells will likely prove critical for long-term immune protection against COVID-19. We here systematically mapped the functional and phenotypic landscape of SARS-CoV-2-specific T cell responses in unexposed individuals, exposed family members, and individuals with acute or convalescent COVID-19. Acute phase SARS-CoV-2-specific T cells displayed a highly activated cytotoxic phenotype that correlated with various clinical markers of disease severity, whereas convalescent phase SARS-CoV-2-specific T cells were polyfunctional and displayed a stem-like memory phenotype. Importantly, SARS-CoV-2-specific T cells were detectable in antibody-seronegative exposed family members and convalescent individuals with a history of asymptomatic and mild COVID-19. Our collective dataset shows that SARS-CoV-2 elicits robust, broad and highly functional memory T cell responses, suggesting that natural exposure or infection may prevent recurrent episodes of severe COVID-19."

[JAMA](#): Association Between Number of In-Person Health Care Visits and SARS-CoV-2 Infection in Obstetrical Patients

"There was no meaningful association between the number of in-person health care visits and the rate of SARS-CoV-2 infection in this sample of obstetrical patients in the Boston area. Massachusetts had the third highest SARS-CoV-2 infection rate in the country during the spring 2020 surge, and the Boston area was particularly affected."

The findings from this obstetrical population who had frequent in-person visits to a health care setting and underwent universal testing for SARS-CoV-2 infection suggest in-person health care visits were not likely to be an important risk factor for infection and that necessary, in-person care can be safely performed. Limitations of this study include the restriction to obstetrical patients. Future studies are needed to determine whether these findings extend to other populations and health care settings."

[PLOS One](#): Impact of cardiovascular risk profile on COVID-19 outcome. A meta-analysis

"This is a meta-analysis of observational studies evaluating cardiovascular (CV) complications in hospitalized COVID-19 patients and the impact of cardiovascular risk factors (RF) or comorbidities on mortality....

Among 77317 hospitalized patients from 21 studies, 12.86% had cardiovascular comorbidities or RF. Cardiovascular complications were registered in 14.09% of cases during hospitalization. At meta-regression analysis, pre-existing cardiovascular comorbidities or RF were significantly associated to cardiovascular complications in COVID-19 patients ($p = 0.019$). Pre-existing cardiovascular comorbidities or RF ($p < 0.001$), older age ($p < 0.001$), and the development of cardiovascular complications during the hospitalization ($p = 0.038$) had a significant interaction with death.

Cardiovascular complications are frequent among COVID-19 patients, and might contribute to adverse clinical events and mortality, together with pre-existing cardiovascular comorbidities and RF. Clinicians worldwide should be aware of this association, to identifying patients at higher risk."

13 August 2020

[Ann Intern Med](#): Contact Settings and Risk for Transmission in 3410 Close Contacts of Patients With COVID-19 in Guangzhou, China

"3410 close contacts of 391 index cases were traced between 13 January and 6 March 2020. Data on the setting of the exposure, reverse transcriptase polymerase chain reaction testing, and clinical characteristics of index and secondary cases were collected....

Among 3410 close contacts, 127 (3.7% [95% CI, 3.1% to 4.4%]) were secondarily infected. Of these 127 persons, 8 (6.3% [CI, 2.1% to 10.5%]) were asymptomatic. Of the 119 symptomatic cases, 20 (16.8%) were defined as mild, 87 (73.1%) as moderate, and 12 (10.1%) as severe or critical. Compared with the household setting (10.3%), the secondary attack rate was lower for exposures in healthcare settings (1.0%; odds ratio [OR], 0.09 [CI, 0.04 to 0.20]) and on public transportation (0.1%; OR, 0.01 [CI, 0.00 to 0.08]). The secondary attack rate increased with the severity of index cases, from 0.3% (CI, 0.0 to 1.0%) for asymptomatic to 3.3% (CI, 1.8% to 4.8%) for mild, 5.6% (CI, 4.4% to 6.8%) for moderate, and 6.2% (CI, 3.2% to 9.1%) for severe or critical cases. Index cases with expectoration were

associated with higher risk for secondary infection (13.6% vs. 3.0% for index cases without expectoration; OR, 4.81 [CI, 3.35 to 6.93])....

Household contact was the main setting for transmission of SARS-CoV-2, and the risk for transmission of SARS-CoV-2 among close contacts increased with the severity of index cases."

12 August 2020

[Clin Microbiol Rev](#): Convalescent Plasma Therapy for COVID-19: State of the Art

"Convalescent plasma (CP) therapy has been used since the early 1900s to treat emerging infectious diseases; its efficacy was later associated with the evidence that polyclonal neutralizing antibodies can reduce the duration of viremia. Recent large outbreaks of viral diseases for which effective antivirals or vaccines are still lacking has renewed the interest in CP as a life-saving treatment. The ongoing COVID-19 pandemic has led to the scaling up of CP therapy to unprecedented levels. Compared with historical usage, pathogen reduction technologies have now added an extra layer of safety to the use of CP, and new manufacturing approaches are being explored. This review summarizes historical settings of application, with a focus on betacoronaviruses, and surveys current approaches for donor selection and CP collection, pooling technologies, pathogen inactivation systems, and banking of CP. We additionally list the ongoing registered clinical trials for CP throughout the world and discuss the trial results published thus far."

ICYMI (In Case You Missed It)

[BMJ Glob Health](#): A checklist to improve health system resilience to infectious disease outbreaks and natural hazards (05 August 2020)

"Recent infectious disease outbreaks, including the ongoing global COVID-19 pandemic and Ebola in the Democratic Republic of the Congo, have demonstrated the critical importance of resilient health systems in safeguarding global health security. Importantly, the human, economic and political tolls of these crises are being amplified by health systems' inabilities to respond quickly and effectively. Improving resilience within health systems can build on pre-existing strengths to enhance the readiness of health system actors to respond to crises, while also maintaining core functions. Using data gathered from a scoping literature review, interviews with key informants and from stakeholders who attended a workshop held in Dhaka, Bangladesh, we developed a Health System Resilience Checklist ('the checklist'). The aim of the checklist is to measure the specific capacities, capabilities and processes that health systems need in order to ensure resilience in the face of both infectious disease outbreaks and natural hazards. The checklist is intended to be adapted and used in a broad set of countries as a component of ongoing processes to ensure that health actors, institutions and populations can mount an effective response to infectious

disease outbreaks and natural hazards while also maintaining core healthcare services. The checklist is an important first step in improving health system resilience to these threats, but additional research and resources will be necessary to further refine and prioritise the checklist items and to pilot the checklist with the frontline health facilities that would be using it. This will help ensure its feasibility and durability for the long-term within the health systems strengthening and health security fields."

[Nature](#): Longitudinal analyses reveal immunological misfiring in severe COVID-19 (posted online 27 July 2020; published 20 August 2020)

"Recent studies have provided insights into the pathogenesis of coronavirus disease 2019 (COVID-19). However, the longitudinal immunological correlates of disease outcome remain unclear. Here we serially analysed immune responses in 113 patients with moderate or severe COVID-19. Immune profiling revealed an overall increase in innate cell lineages, with a concomitant reduction in T cell number. An early elevation in cytokine levels was associated with worse disease outcomes. Following an early increase in cytokines, patients with moderate COVID-19 displayed a progressive reduction in type 1 (antiviral) and type 3 (antifungal) responses. By contrast, patients with severe COVID-19 maintained these elevated responses throughout the course of the disease. Moreover, severe COVID-19 was accompanied by an increase in multiple type 2 (anti-helminths) effectors, including interleukin-5 (IL-5), IL-13, immunoglobulin E and eosinophils. Unsupervised clustering analysis identified four immune signatures, representing growth factors (A), type-2/3 cytokines (B), mixed type-1/2/3 cytokines (C), and chemokines (D) that correlated with three distinct disease trajectories. The immune profiles of patients who recovered from moderate COVID-19 were enriched in tissue reparative growth factor signature A, whereas the profiles of those who developed severe disease had elevated levels of all four signatures. Thus, we have identified a maladapted immune response profile associated with severe COVID-19 and poor clinical outcome, as well as early immune signatures that correlate with divergent disease trajectories."

Selected Literature: Preprints

Preprints are found on preprint servers such as [arXiv](#), [bioRxiv](#), and [medRxiv](#); they are commonly used for biomedical research. Per medRxiv:

"Preprints are preliminary reports of work that have not been certified by peer review. They should not be relied on to guide clinical practice or health-related behavior and should not be reported in news media as established information."

Preprints may later be published in peer-reviewed journals.

[medRxiv](#): RNA-Based COVID-19 Vaccine BNT162b2 Selected for a Pivotal Efficacy Study (20 August 2020)

Note: This is about the Pfizer BioNTech COVID-19 vaccine.

"Background: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections and the resulting disease, coronavirus disease 2019 (COVID-19), have spread to millions of people globally. Multiple vaccine candidates are under development, but no vaccine is currently available.

Methods: Healthy adults 18–55 and 65–85 years of age were randomized in an ongoing, placebo-controlled, observer-blinded dose-escalation study to receive 2 doses at 21-day intervals of placebo or either of 2 lipid nanoparticle-formulated, nucleoside-modified RNA vaccine candidates: BNT162b1, which encodes a secreted trimerized SARS-CoV-2 receptor-binding domain, or BNT162b2, which encodes a prefusion stabilized membrane-anchored SARS-CoV-2 full-length spike. In each of 13 groups of 15 participants, 12 received vaccine and 3 received placebo. Groups were distinguished by vaccine candidate, age of participant, and vaccine dose level. Interim safety and immunogenicity data of BNT162b1 in younger adults have been reported previously from US and German trials. We now present additional safety and immunogenicity data from the US Phase 1 trial that supported selection of the vaccine candidate advanced to a pivotal Phase 2/3 safety and efficacy evaluation.

Results: In both younger and older adults, the 2 vaccine candidates elicited similar dose-dependent SARS-CoV-2-neutralizing geometric mean titers (GMTs), comparable to or higher than the GMT of a panel of SARS-CoV-2 convalescent sera. BNT162b2 was associated with less systemic reactogenicity, particularly in older adults.

Conclusion: These results support selection of the BNT162b2 vaccine candidate for Phase 2/3 large-scale safety and efficacy evaluation, currently underway."

[bioRxiv](#): Seeding of outbreaks of COVID-19 by contaminated fresh and frozen food (posted 18 August 2020)

"An explanation is required for the re-emergence of COVID-19 outbreaks in regions with apparent local eradication. Recent outbreaks have emerged in Vietnam, New Zealand and parts of China where there had been no cases for some months. Importation of contaminated food and food packaging is a feasible source for such outbreaks and a source of clusters within existing outbreaks. Such events can be prevented if the risk is better appreciated."

[medRxiv](#): Impacts on Surgery Resident Education at a first wave COVID-19 epicenter (posted 18 August 2020)

"Background: This study aims to identify the effects of the COVID-19 pandemic on surgical resident training and education at Danbury Hospital.

Methods: We conducted an observational study at a Western Connecticut hospital heavily affected by the first wave of the COVID-19 pandemic to assess its effects on surgical residents, focusing on surgical education, clinical experience, and operative skills development. Objective data was available through recorded work hours, case logs, and formal didactics. In addition, we created an anonymous survey to assess resident perception of their residency experience during the pandemic.

Results: There are 22 surgical residents at our institution; all were included in the study. Resident weekly duty hours decreased by 23.9 hours with the majority of clinical time redirected to caring for COVID-19 patients. Independent studying increased by 1.6 hours (26.2%) while weekly didactics decreased by 2.1 hours (35.6%). The operative volume per resident decreased by 65.7% from 35.0 to 12.0 cases for the period of interest, with a disproportionately high effect on junior residents, who experienced a 76.2% decrease. Unsurprisingly, 70% of residents reported a negative effect of the pandemic on their surgical skills.

Conclusions: During the first wave of the COVID-19 pandemic, surgical residents' usual workflows changed dramatically, as much of their time was dedicated to the critical care of patients with COVID-19. However, the consequent opportunity cost was to surgery-specific training; there was a significant decrease in operative cases and time spent in surgical didactics, along with elevated concern about overall preparedness for their intended career."

[medRxiv](#): Longitudinal SARS-CoV-2 serosurveillance of over ten thousand health care workers in the Providence Oregon cohort (posted 18 August 2020)

"Frontline healthcare workers (HCW) are a high-risk population for SARS-CoV-2 infection. Here we present results from a large serosurveillance study of 10,019 asymptomatic HCW conducted during April-May 2020, in eight hospital medical centers across the state of Oregon, USA during the initial peak of the pandemic. Free and voluntary testing was performed at 14 +/- 3 day intervals, over a 4-week window at each site, utilizing a lab-developed ELISA based on the Eitope Diagnostics COVID-19 nucleocapsid IgG detection Kit. We identified 253 SARS-CoV-2 IgG seropositive individuals among 10,019 total participants, representing a cross-sectional seroprevalence of 2.53%. Subgroup analysis identified differential seropositivity by job role, ranging from 8.03% among housekeepers, odds ratio 3.17 (95% CI 1.59-5.71), to 0.00% among anesthesiologists, odds ratio 0.00 (95% CI 0-0.26), both of which were significant. Over the course of the study, 17 seroconversions (0.25%) and 101 seroreversions (1.50%) were identified. Self-reported SARS-CoV-2 swab qPCR

testing, when compared with subsequent serology on study, showed only modest agreement, $\kappa = 0.47$ (95% CI 0.32-0.62). Overall, these findings demonstrate relatively low seroprevalence and very low seroconversion rates among HCW in Oregon, USA, over a period in which aggressive social distancing measures were in place. The high rate of seroreversion observed in this cohort, and the relatively high discordance between SARS-CoV-2 serology and swab qPCR, highlight limitations of current detection methods, and stress the need for development of novel assessment methodologies to more accurately identify exposure (and/or immunity) to SARS-CoV-2 in this population."

Information Sources: Treatment Trackers

There are a lot of potential drugs or other compounds – some good, some not so good or downright odd – being mentioned as treatments for COVID-19. These trackers provide a way to see what is under development and currently being studied in trials, and overlap somewhat with vaccines:

- [COVID-19 therapeutic development tracker](#) (Bio)
- [Coronavirus drug and treatment tracker](#) (NYT)
- [COVID-19 therapeutics tracker](#) (RF)
- [Covid-19 drugs & vaccines tracker](#) (STAT)
- [COVID-19 treatment and vaccine tracker](#) (FasterCures)

News in Brief

Earlier this week, Texas became the 4th state (joining NY, NJ, and CA) to surpass 10,000 COVID-19 deaths ([Texas Tribune](#)). A few days later, Florida became the 5th state ([Miami Herald](#)).

"COVID is now the No. 3 cause of death in the US – ahead of accidents, injuries, lung disease, diabetes, Alzheimer's, and many, many other causes," said Dr. Thomas Frieden, a former director of the Centers for Disease Control and Prevention ([CNN](#)).

A survey of physicians in the US finds that 86% think the pandemic won't be under control until January 2021 and 46% think it won't be under control until after June 2021 ([PF](#); read the [full report \[pdf\]](#))

Long read: "Long-haulers are redefining COVID-19" ([Atlantic](#))

Transmission and Testing

Can air conditioners spread COVID-19? Well, it's complicated ([NPR](#)).

The FDA has approved a saliva test for the coronavirus ([STAT](#)).

Dogs are helping develop quicker, more accurate tests for coronavirus ([WaPo](#)). (Bonus content: article includes photos of dogs in action.)

A new Executive Order rescinds requirements to have FDA review of and approval for laboratory tests for COVID-19 ([HHS](#)).

Long read: "'It's the Hunger Games for laboratories.' Why some people are waiting weeks for their COVID-19 test results" ([Time](#))

Data Integrity

Prisons and detention centers account for all of the top 10 COVID-19 outbreak clusters in the US, but data – especially on race – are unclear ([STAT](#)).

"A new U.S. intelligence report says top officials in Beijing were in the dark in early January on the true dangers of the virus" ([NYT](#)).

Treatments

The FDA has put a hold on the emergency approval of convalescent plasma as a treatment for COVID-19, citing "weak data" ([NYT](#)).

There are suggestions that a botanical extract from the oleander plant could treat or even "cure" COVID-19 ([Medpage](#)). This post from a medical ethnobotanist from Emory University provides some background on oleandrin ([Conversation](#)).

See also the COVID-19 drugs and therapeutic trackers noted above.

Vaccines

A new directive for HHS preempts restrictions in all 50 states and allows pharmacists to give childhood vaccinations ([AP](#)).

Operation Warp Speed is on track to have a COVID-19 vaccine ready by the end of the year ([DOD](#)).

We don't know if COVID-19 vaccines will be safe for children or pregnant women because data are lacking ([STAT](#)).

"Vaccines use bizarre stuff" – before we can have a COVID-19 vaccine, we have to procure rare ingredients, stabilize the supply chain, and test manufacturing processes ([Bloomberg](#)).

Ripple Effects

Some patients who recovered from COVID-19 are facing stigma: "People act like you did something to catch it, or you did something wrong, and that's why you got it... I feel like I have a scarlet letter on my chest." ([NBC](#))

"Staying strong during lockdown means reaching out — and working your mind, too" ([NPR](#)).

Looking for some mental stimulation? NMCP Library Services has fiction, nonfiction, biographies, and children's books (in print or audio), along with DVDs and Blurays available for loan. If you can't physically get to the library, check out the [Navy's MWR Digital Library](#) for ebooks, audios, and more – learn a new language with Mango or listen to Great Courses to expand your knowledge.

Back to School

As many colleges and universities welcome students back to campus, some are suspending in-person classes as coronavirus outbreaks pop up ([NPR](#)).

Medical school applications are up, even though the number of slots is relatively unchanged ([Medpage](#)).

Long read: "What we've stolen from our kids" ([Atlantic](#)).

COVID Infodemic

Doctors aren't just dealing with a viral pandemic, but also viral misinformation; patients are more inclined to believe what they read on Facebook over what a medical professional tells them ([NYT](#)).

Here is a round-up of 9 COVID-19 persistent myths and false claims you may encounter ([SciAm](#)).

One possible complication for accuracy and authoritativeness with COVID-19 is the readability level of official public health information. A new study found 95% of the websites evaluated had reading levels about eighth grade level – the level recommended by the AMA, NIH, and CDC – on 5 different metrics ([JAMA Netw Open](#)).

It also doesn't help that Facebook and its algorithm are a major source of "superspreader" health misinformation ([Avaaz](#)).

Long read: "How QAnon rode the pandemic to new heights — and fueled the viral anti-mask phenomenon" ([NBC](#))

Thanks, Coronavirus

The National Health and Nutrition Examination Survey (NHANES) was suspended in March because of the pandemic, and while collection has started back, it is limited. Experts are concerned about a smaller overall sample and delay in release of data. NHANES is a huge dataset that impacts health policy and public health initiatives for years to come ([Medpage](#)).

The pandemic is impacting how people get around; walking, biking, and driving are in, using public transportation or Uber are out ([NPR](#)).

Other Infectious Diseases and Outbreaks

In an effort to counteract *Aedes aegypti* spread of diseases such as dengue fever and Zika, officials has approved plans to release hundreds of millions of genetically engineered mosquitoes in Florida ([Newsweek](#)).

Massachusetts public health officials announced a second human case of Eastern Equine Encephalitis ([MA DPH](#)).

A resident of South Lake Tahoe has tested positive for plague ([CDPH](#)).

The CDC warns that an outbreak of *Salmonella* enteritidis infections are linked to bagged peaches ([CDC](#)).

For the Fauci Fans

According to reports, Dr. Fauci is "doing ok" after surgery to remove a polyp from his vocal cord; he will have to limit talking to allow for recovery ([Medpage](#)).

In case you need a Fauci fix or maybe some swag for your office, the National Bobblehead Hall of Fame and Museum (yes, [that's a real thing](#)) has a Dr. Fauci model ([standard](#) or [facepalm](#)) available for preorder. A portion of sales are donated to [Protect the Heroes Campaign](#) in support of front line heroes and providing PPE ([Medpage](#); [BHOF](#)).

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